



Original communication

Concentrations of drugs determined in blood samples collected from suspected drugged drivers in England and Wales

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ABSTRACT

This communication reports the blood concentrations of alcohol and drugs from 376 cases of alleged driving under the influence of drugs analysed at the Forensic Science Service Chorley and London laboratories between February 2010 and March 2011. The samples were analysed for alcohol, amphetamine, benzodiazepines, cocaine, MDMA, opiates, γ -hydroxybutyrate (GHB), ketamine, methadone and methylmethcathinone (the 4-isomer of which is known as mephedrone). The results were interpreted with respect to the number and type of drugs of abuse detected and the concentrations measured. Alcohol was quantified in 113 cases (30%), and of these a level in excess of the prescribed UK limit for driving of 80 mg% was present in 90 cases. In 80 cases, only the concentration of alcohol was measured, the concentrations of both drugs and alcohol were measured in 33 cases. In the remaining 263 cases, only the concentrations of relevant drugs of abuse were measured. The most common drug of abuse quantified was cocaine which was detected in 92 cases, either as the active drug or as its major metabolite benzoylecgonine, followed by diazepam which was quantified in 76 cases. Concentrations of some new drugs, and drugs rarely reported in driving under the influence cases are also presented.

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1. Introduction

A number of cases of alleged driving under the influence of drugs were analysed by the Forensic Science Service (FSS) in the UK during the period February 2010 to March 2011. The legislation related to drug driving in the UK is defined in the Road Traffic Act 1988 where section 4 makes it an offence to drive, or attempt to drive, a mechanically propelled vehicle whilst unfit through drink or drugs.

A suspected drug-impaired driver normally commits a moving traffic offence (e.g. speeding, weaving, failing to stop at traffic lights etc.) or is involved in a road traffic collision before they are apprehended by police in England & Wales. Drivers are normally required to co-operate with a roadside screening test for alcohol. If the result of this test indicates the driver is below the breath alcohol limit for driving, but they are still displaying signs of intoxication (e.g. slurred speech, clumsiness), strange behaviour (e.g. agitation or hostility) or they have a history of criminal drug abuse, they may be asked to participate in a field impairment test (FIT).¹ Only

specifically trained traffic police officers may conduct this test and if the driver performs poorly they may be arrested under suspicion of driving whilst impaired through drink or drugs. In the final stage of the process, the suspect is assessed by a Forensic Medical Examiner (FME) who will determine whether their condition is due to a drug, rather than an underlying medical condition or fatigue. A sample of blood or urine is then collected from the driver and sent for analysis. Whilst the presence of drugs is frequently confirmed in cases of suspected drug-driving, a conviction for this offence relies on the demonstration of impairment on the part of the driver at the time of the incident. The FIT and FME opinion may provide evidence of the driver being under the influence of drugs, however they do not necessarily demonstrate driving impairment.

While there has been a considerable amount of research into the prevalence of drink driving in the UK, very little research has focused on driving under the influence of drugs.² A small number of studies have looked at the prevalence of drug driving,^{3,4} and the contribution of drugs to road traffic fatalities,^{5,6} with the most relevant research originating from Scotland.^{2,6–9} However, there is very little published data on the actual concentrations of drugs found in drivers apprehended in the UK. Some data has been gathered for drivers under the influence of benzodiazepines and opiates,¹⁰ and amphetamine and methylenedioxymethylamphetamine (MDMA),¹¹ but this has not been published. Two studies reporting blood

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concentrations in drug-impaired drivers in Scotland were published in 1999,^{7,12} but there is currently no corresponding published data for drug-impaired drivers in England & Wales. Knowledge of the concentration of a psychoactive drug in blood is necessary to enable valid conclusions to be drawn about any pharmacological effects produced. A more detailed analysis which goes beyond prevalence would enable the identification of cases where the drugs detected were above therapeutic concentrations. This is important as it is currently unclear from the existing UK drug-driving data what proportion of the opiates and benzodiazepines detected have been prescribed and what proportion are being used illicitly.²

Internationally, publication of the concentrations of drugs found in drivers is much more widespread. In Sweden, concentrations of cocaine and its metabolite benzoylecgonine (BZE),¹³ amphetamine,^{14,15} benzodiazepines,¹⁶ opiates¹⁷ and γ -hydroxybutyrate (GHB)^{18,19} in drug-impaired drivers have been reported. There is also information in the literature concerning concentrations of benzodiazepines^{20,21} and methadone²² found in drivers in Norway, GHB found in drug-driving cases in the USA,²³ and of amphetamine in drivers in Finland.²⁴ Concentrations of amphetamine²⁵ and various other drugs found in drivers in the Netherlands²⁶ and Switzerland²⁷ have also been published.

In this communication, we report the concentrations of alcohol and illicit and certain prescription drugs found in whole blood samples taken from 376 alleged drug-impaired drivers in England & Wales. Our study also includes concentrations of less common drugs of abuse, such as alprazolam, GHB and ketamine, and the previously termed 'legal' high mephedrone, as well as phenazepam, found in drivers in England & Wales. We believe that this is an important area of research as there is very little data on the prevalence or concentrations of these drugs in drivers, despite recent surveys and anecdotal evidence suggesting there has been a surge in their use.²

2. Study protocol

All alleged drug-driving samples submitted to the FSS undergo an initial screening for five classes of abused drugs: amphetamines/methylamphetamines, benzodiazepines, cocaine and/or cocaine metabolites, opiates and cannabinoids, which comprise the so-called 'standard panel' of drugs. Samples are also specifically screened for methadone (and morphine in the case of positive opiates screening result). If requested, alcohol analysis is also carried out. Where the results of the screening test are positive for more than one drug type, normally only one drug is chosen for confirmation, as permitted by police contracts. This decision is based on a number of factors including the approximate concentration of each positive drug type, the time delay between driving and sampling, the behaviour of the driver if recorded by the police, the legislative class of the drugs indicated and any additional intelligence (e.g. drugs found in the car or in the driver's possession). If the alcohol concentration is in excess of the prescribed limit for driving in the UK (80 mg of alcohol in 100 mL blood) positive drug screening results are not usually confirmed, unless a fatality has occurred.

Of the 1100 samples received by the FSS in alleged drug-driving cases from February 2010 to March 2011, only 376 cases met the criteria for this study. Our criteria stated that eligible cases must:

- (a) be standard drug-driving cases only (i.e. no fatalities linked to the case),
- (b) be accompanied by a blood sample.
- (c) contain a measured level of drug(s).

For this subset of cases we have recorded the concentrations of amphetamine, MDMA, cocaine, BZE, diazepam, nordiazepam, oxazepam, temazepam, morphine, codeine, dihydrocodeine,

methadone, mephedrone, GHB, phenazepam and ketamine confirmed to be present. The concentrations of cannabinoids found in whole blood samples are not measured, so these cases do not form part of our study. All of the samples in this study were analysed at either the London or Chorley laboratories of the FSS, having been submitted in cases of alleged drug driving by 26 of the 34 police forces in England & Wales.

3. Methods

3.1. Blood sampling

A variety of sample vials is used in the United Kingdom. Samples taken at hospital will frequently be unpreserved; those in police stations will mostly be preserved with sodium fluoride and would typically be of volume 3–6 mL.

3.2. Sample storage

Once received at the laboratory all samples were kept refrigerated. Ideally, all submitted samples should have been preserved with a fluoride concentration of at least 1.5% weight/volume, because it is well documented that the presence of micro-organisms can result in an unreliable alcohol result.²⁸ Cocaine²⁹ and mephedrone³⁰ also break down in whole blood, although the presence of fluoride somewhat inhibits the process. If it was unclear whether or not fluoride was present in the sample, the fluoride concentration was determined by means of a fluoride-sensitive electrode.

3.3. Alcohol analysis

Alcohol was analysed using gas chromatography with flame ionisation detection (GC-FID) using c. 300 μ L of sample. The analysis was carried out in duplicate on two different GC columns to rule out the presence of any interfering volatile substances. The average of the two results was calculated, and a deduction of 6 mg/100 mL (mg%) for results <100 mg%, or 6% for results >100 mg% was taken from the average measured value. This allows for any uncertainty in the measurements and the result is reported as the 'not less than' value rather than the actual measured value.³¹

3.4. Initial screening

Initial screening, using 150 μ L of sample with subsequent dilution as per kit insert, was conducted by means of enzyme immunoassay (EIA) using kits supplied by Concateno® (formerly Cozart®) and Orasure® Technologies Inc. The drugs of abuse covered by this screen and the positive cut-off concentrations for each type in whole blood are outlined in Table 1.

3.5. Confirmation

Where we elected to confirm a positive EIA result, this was done using an extraction and derivatisation method followed by either

Table 1

The EIA screening tests and cut-off concentrations for drugs of abuse used in this study.

Drug type	Specific drug antibody used	Cut-off (ng/mL)
Amphetamine	Amphetamine	25
Benzodiazepines	Oxazepam	50
Cocaine/BZE	BZE	50
Methadone	Methadone	25
Methylamphetamines	Methylamphetamine	50
Opiates	Morphine	25

gas chromatography-mass spectrometry (GC–MS) or high-performance liquid chromatography (HPLC) with diode array detection. Not every drug type listed in Table 1 is commonly confirmed in alleged drug-driving cases. For example, although frequently positive at the screening stage, methadone is rarely confirmed because the driver is usually indicated by police to be a prescription user and hence likely to have developed significant tolerance to the effects of methadone.³²

Analysis for drugs not included in the standard panel was performed if the police suspected certain drugs e.g. mephedrone, GHB or ketamine and/or the results from the standard panel were negative or negligible.

4. Results

4.1. Alcohol

Alcohol was quantified in the laboratory either alone or with drugs of abuse in 113 of the 376 cases (30%). The distribution of blood alcohol concentrations is shown in Fig. 1. The x-axis ranges are based on the UK sentencing guidelines for drink-driving offences.³³ Blood alcohol concentrations were most commonly between 81 and 137 mg%. The mean and median blood alcohol concentrations were 120 and 110 mg%, respectively.

Some samples would have been submitted for drug analysis without there having been a roadside breath test for alcohol; others may have been submitted through lack of knowledge of the correct police procedures. The prevalence of alcohol in drug-impaired drivers is underestimated in this study as we have only included results where the concentration of alcohol was measured in the laboratory, and not where it was confirmed to be present by means of an evidential breath test before the blood sample was taken, where breath analysis would remain the evidential sample.

4.2. Drugs of abuse

A breakdown of the drugs of abuse for which concentrations were measured in this study is shown in Fig. 2. As 81 of the 376 samples contained only alcohol, the total number of cases reflected in Fig. 2 is 295. The most common drug quantified was cocaine and/or its major metabolite benzoylecgonine (BZE) followed by diazepam and its metabolite nordiazepam. Table 2 presents the

detected substances and their reported concentrations in the whole blood samples. Table 2 and Fig. 2 show the total incidence of individual drugs in the study. It is important to note that these individual drug occurrences cannot be added together to represent the total percentage drug incidence in the population, as this would result in double counting of drug incidence for cases of multiple drug use.

4.2.1. Amphetamine

Amphetamine is an illicit stimulant (and a class B controlled drug in the UK) and drivers under its influence often display a propensity for speeding, failing to stop, and a lack of attention.³⁴ Amphetamine was quantified in 39 blood samples in this study and the frequency distribution of the concentrations of amphetamine is shown in Fig. 3. The mean and median concentrations are 496 and 360 ng/mL, respectively. Methylenedioxymethylamphetamine was not detected in any of the cases in this study.

4.2.2. Methylenedioxymethylamphetamine

Drivers under the influence of the stimulant methylenedioxymethylamphetamine (MDMA, a class A controlled substance in the UK), known as ‘ecstasy’, may be prepared to accept higher levels of risk, and the psychotropic properties and secondary effects of the drug (i.e. fatigue) are incompatible with safe driving.³⁵ MDMA was quantified in eight blood samples and the mean and median concentrations of MDMA in whole blood are 256 and 230 ng/mL, respectively. The presence of the major active metabolite of MDMA, methylenedioxyamphetamine (MDA), was quantified alongside MDMA in only one case, at a concentration of 50 ng/mL.

4.2.3. Benzodiazepines

Benzodiazepines are prescription-only medications and class C controlled drugs in the UK. The sedative and hypnotic effects of benzodiazepines can significantly impair safe driving by slowing reaction times and causing lane deviation,³⁶ and patients prescribed benzodiazepines should normally be warned not to drive or operate machinery and to avoid alcohol; this warning is reinforced on the tablet container. In this study, when a positive indication for benzodiazepines on the EIA screen is chosen for confirmation, a GC–MS screen is subsequently carried out on the sample. The EIA kits cross react primarily with diazepam, desmethyldiazepam, temazepam and oxazepam, although high concentrations of nitrazepam, alprazolam and midazolam may also produce a positive response. The subsequent GCMS screen can identify high-dose benzodiazepines (e.g. diazepam, nordiazepam, nitrazepam, temazepam and oxazepam) as well as low-dose benzodiazepines (e.g. alprazolam, flunitrazepam and midazolam). The concentrations of benzodiazepines present are then quantified using HPLC or GC–MS as appropriate. Although a wide range of benzodiazepines may be identified using the GC–MS screen, only a limited number are routinely seen in drug-driving cases in this laboratory.

Diazepam was quantified in 76 samples following GC–MS screening (78% of benzodiazepine-positive cases), and in 73 of those cases diazepam was present alongside its active metabolite nordiazepam (74%). The frequency distribution for both drugs can be seen in Fig. 4. The mean and median concentrations of diazepam are 895 and 560 ng/mL, respectively. The mean and median concentrations of nordiazepam are 1013 and 575 ng/mL, respectively.

The ratio of diazepam to nordiazepam can provide useful information on the dosing pattern for diazepam,¹⁶ and the distribution of diazepam : nordiazepam ratios measured in this study is presented in Fig. 5.

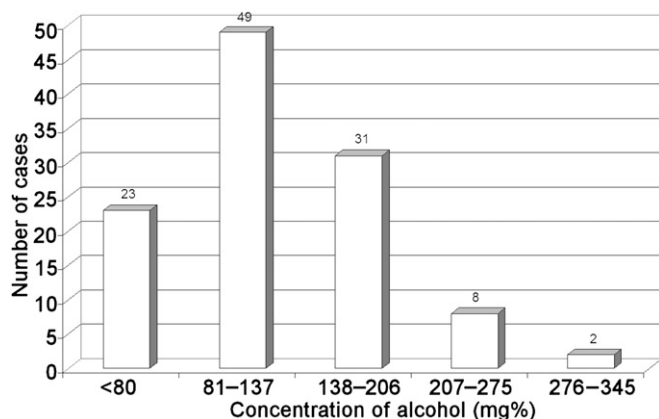


Fig. 1. Frequency distribution of alcohol concentrations found in this study ($N = 112$). The x-axis ranges correspond to the boundary sentencing levels for drink-driving offences in the UK³²: a blood alcohol concentration of 81–137 mg% corresponds to a 12–16 month disqualification; 138–206 mg%, 12–22 month disqualification; 207–275 mg%, 23–28 month disqualification and 276–345 mg%, 29–36 month disqualification.

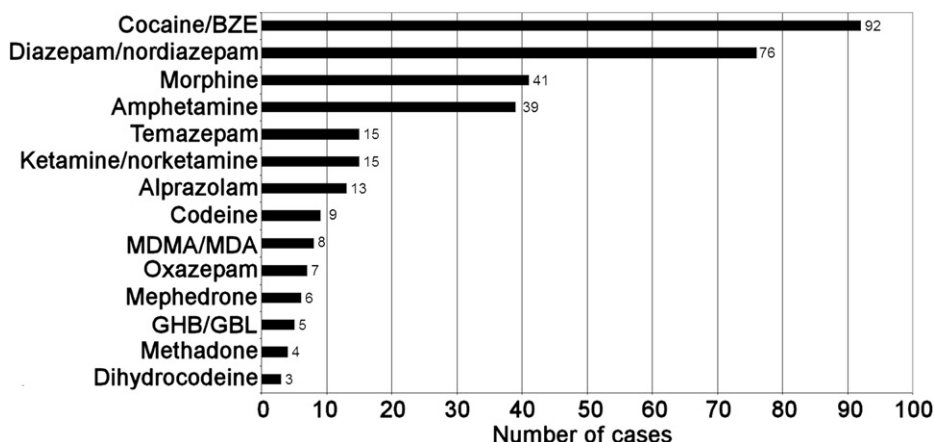


Fig. 2. Breakdown of the drugs of abuse detected in this study ($N = 296$).

Oxazepam was quantified in seven samples following GC–MS screening (7% of benzodiazepine-positive cases) with mean and median concentrations of 391 and 370 ng/mL.

Temazepam was quantified in 15 samples following GC–MS screening (15% of benzodiazepine-positive cases) with mean and median concentrations of 1242 and 400 ng/mL, respectively.

Alprazolam was quantified in 13 samples following GC–MS screening (13% of benzodiazepine-positive cases) and the mean and median concentrations are 141 and 70 ng/mL, respectively.

4.2.4. Cocaine

Cocaine is a stimulant which has been shown to produce a distracting intoxicating euphoria, and aggressive and impulsive behaviour in drivers.³⁷ Evidence of cocaine use was quantified in 92 samples overall, although the method does not differentiate between 'crack' cocaine and cocaine hydrochloride use. Cocaine was quantified as the active drug alongside its inactive metabolite BZE in 44 cases, or as BZE alone in 48 cases; cocaine was not

quantified alone in this study. The distribution of the concentrations of cocaine can be seen in Fig. 6, and the concentrations of BZE in Fig. 7. The mean and median concentrations of cocaine are 53 and 25 ng/mL, respectively ($N = 44$). Although cocaine was not identified without BZE also being present, BZE was frequently present in blood when cocaine was not present or the concentration of cocaine was too low to be detected.

The overall mean and median concentrations of BZE are 677 and 420 ng/mL. The mean concentration of BZE was higher when detected with cocaine than when detected alone (1013 vs. 355 ng/mL). However, the presence of BZE alone could be indicative of the user being in the come-down or 'crash' phase of cocaine use, and the effects experienced by the user during this period (e.g. fatigue and lack of concentration) make it a particularly dangerous time for driving.³⁷

4.2.5. Opiates

Opiates are centrally acting drugs that produce not only analgesia but a number of side-effects including impaired concentration and co-ordination both of which can negatively influence driving ability.³⁸ The use of morphine itself is also associated with an increased crash risk,^{39,40} and patients prescribed opiates should normally be warned not to drive or operate machinery and to avoid alcohol; this warning is reinforced on the tablet container. Morphine (a class A controlled drug in the UK) was detected as the parent drug (known as 'free morphine') in this study.

Table 2

Blood concentrations for each drug type in ng/mL (except *: $\mu\text{g/mL}$).

Drug	N	Mean	Median	Maximum	Minimum
<i>Benzodiazepines</i>					
Alprazolam	13	141	70	400	50
Diazepam	76	895	560	6400	20
Nordiazepam	73	1013	575	6400	10
Diazepam:nordiazepam	73	2.91	0.92	25.00	0.20
Oxazepam	7	391	370	1000	170
Temazepam	15	1242	400	5000	70
<i>Amphetamines</i>					
Amphetamine	39	496	360	1600	60
MDMA	8	256	230	460	140
MDA	1	—	—	50	50
<i>Opiates</i>					
Codeine	9	348	60	2300	12
Dihydrocodeine	3	410	190	1000	40
Morphine	41	66	40	390	10
Morphine:codeine	6	3.20	2.19	8.00	0.05
<i>Cocaine</i>					
Cocaine	44	53	25	400	4
Benzoylcegonine (all cases)	92	677	420	6000	40
Benzoylcegonine (with cocaine)	45	1013	740	6000	110
Benzoylcegonine (only)	48	355	230	1700	40
<i>Other drugs</i>					
Ketamine	14	421	385	850	170
Norketamine	14	605	410	1400	190
Mephedrone	6	161	83	370	39
Methadone	4	305	290	440	70
GHB/GBL*	5	126	120	190	80

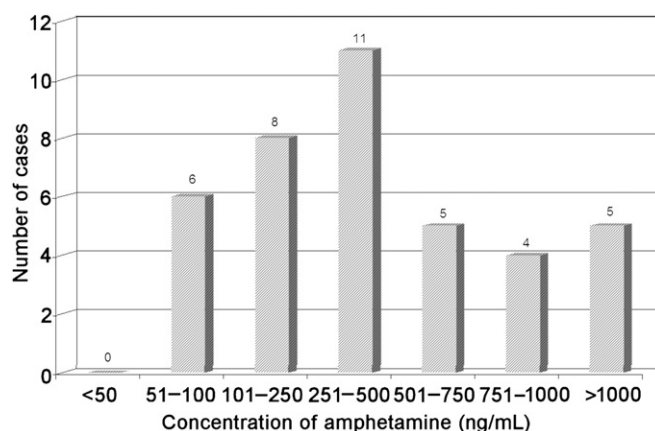


Fig. 3. Frequency distribution of the levels of amphetamine detected in whole blood ($N = 39$).

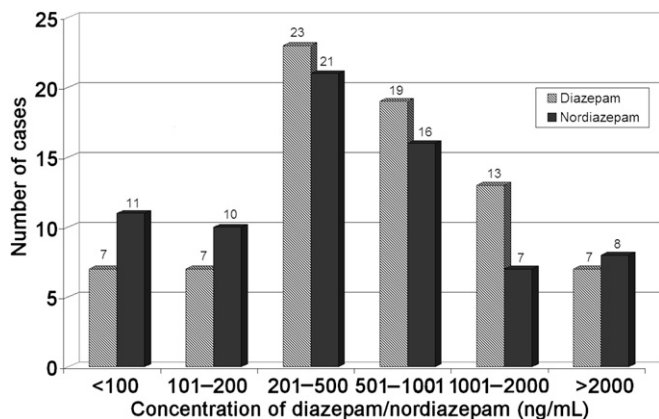


Fig. 4. Frequency distribution of the levels of diazepam and nordiazepam detected in whole blood ($N = 76$ diazepam, $N = 73$ nordiazepam).

Fig. 8 shows the concentrations of free morphine encountered in the 41 positive samples in this study; the mean and median concentrations of morphine are 66 and 40 ng/mL, respectively. In one case, the driver was given morphine as part of emergency treatment (giving a concentration of 40 ng/mL). However, where the circumstances of the case indicate the driver was given medical treatment in hospital, morphine concentrations are not usually measured.

Codeine (a class B controlled drug in the UK, except for over-the-counter preparations containing <100 mg codeine⁴¹) was present in nine whole blood samples as free codeine and the mean and median concentrations are 348 and 60 ng/mL, respectively. Morphine and codeine were quantified together in six cases and the morphine-to-codeine ratios were 0.05, 0.09, 0.88, 3.50, 6.67 and 8.00. The relevance of these ratios is considered later.

Dihydrocodeine (a class B controlled drug in the UK except for over-the-counter preparations containing <100 mg dihydrocodeine⁴¹) was present in three samples at concentrations of 40, 190 and 1000 ng/mL. The mean and median concentrations of dihydrocodeine are 410 and 190 ng/mL, respectively.

4.2.6. Mephedrone

4-Methylmethcathinone (also known as 'mephedrone') is a new drug of abuse that has become popular in the UK. It is one of a growing number of chemical compounds developed and

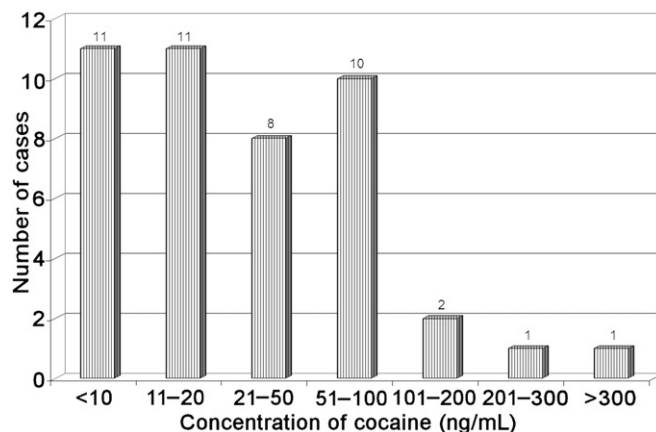


Fig. 6. Frequency distribution of the concentrations of cocaine found in this study ($N = 44$).

marketed to supply the drug dance scene culture and attempt to circumvent current drug controls.⁴² Previously known as a 'legal high', it was designated a controlled (class B) substance in the UK in 2010. Mephedrone produces a number of effects which may affect driving, including poor concentration, hallucinations and psychosis. The analytical technique for mephedrone used in our Toxicology laboratory is capable of detecting the three compounds 2-, 3- and 4-methylmethcathinone but we are unable to distinguish between them. However, the only form of the drug encountered in the FSS drugs laboratory, which can distinguish the isomers using NMR, is 4-methylmethcathinone.

Mephedrone was quantified in six cases in this study, and the concentrations and associated case information are given in Table 3. The mean and median concentrations of mephedrone measured in this study are 161 and 83 ng/mL.

4.2.7. GHB

GHB (a class C controlled drug in the UK) is abused for its intoxicating euphoric effects and by bodybuilders as an alternative to steroids. It has also been associated with drug-facilitated sexual assault. As it is a central nervous system depressant it can affect driving by causing slowed reaction times and drowsiness.²³

A recreational dose of GHB can result in impairment of cognitive and psychomotor functioning which is not compatible with the performance of skilled tasks such as driving.²³ The detection

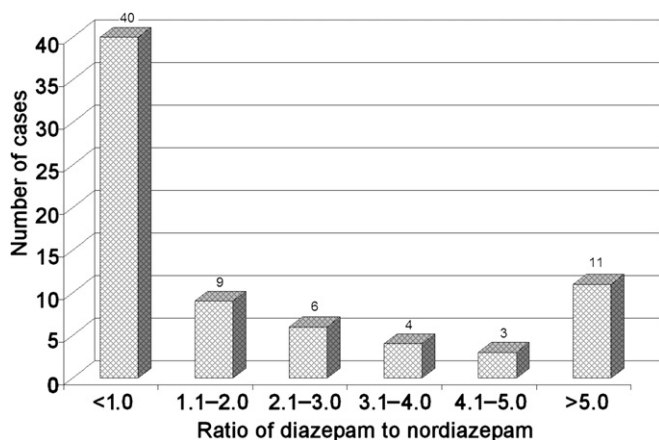


Fig. 5. Frequency distribution of the ratios of diazepam to nordiazepam detected in whole blood ($N = 73$).

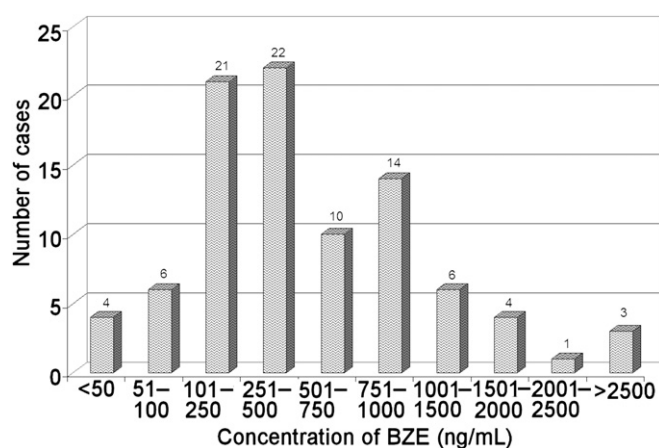


Fig. 7. Frequency distribution of the concentrations of BZE found in this study ($N = 92$).

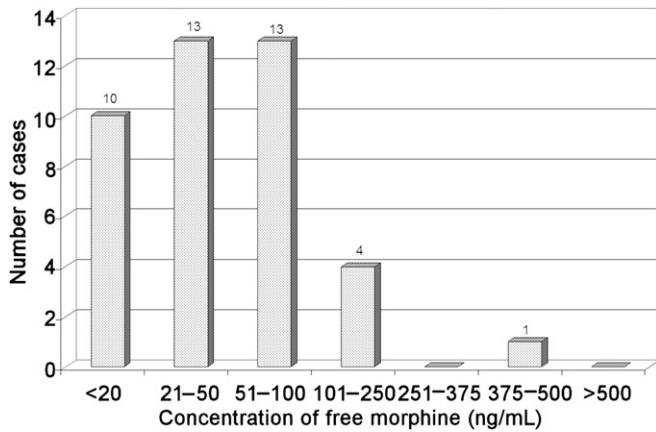


Fig. 8. Frequency distribution of concentrations of free morphine found in this study ($N = 41$).

method for GHB in this laboratory is based on the conversion of GHB to γ -butyrolactone (GBL) therefore we are unable to establish whether drivers testing positive for GBL have consumed GHB, GBL or the precursor 1,4-butanediol (which is converted to GHB in the body) or a combination of these drugs. GHB was quantified in five whole blood samples in this study and the concentrations and associated case details are given in Table 4. The mean and median concentrations measured are 126 and 120 $\mu\text{g/mL}$, respectively.

4.2.8. Ketamine

Ketamine is an anaesthetic and analgesic with hallucinogenic effects and a controlled substance in the UK (class C). Although its affect on driving remains to be observed^{34,43} it is likely to be negative.^{44,45} A 100 mg dose of ketamine is usually enough to enter what is known as a 'K-hole' state giving the user a sense of well-being, hallucinations, feelings of alternate consciousness and 'out-of-body' experiences.⁴⁵ Ketamine and its major metabolite norketamine were quantified in 14 cases and the concentrations and associated case details are given in Table 5. The mean and median concentrations of ketamine are 421 and 385 ng/mL, respectively, and the mean and median norketamine concentrations are 605 and 410 ng/mL.

4.2.9. Methadone

Methadone is a synthetic opioid analgesic (class A controlled drug in the UK) which is available on prescription for the treatment of opiate dependence. Although methadone can produce effects which can impair driving, such as sedation, drowsiness and confusion, the normal range of doses given orally for methadone

maintenance is unlikely to impair driving performance. However, abuse of methadone and doses given to relieve chronic pain, especially to naïve users, have the potential to impair driving.³⁹

Methadone was quantified in four blood samples at concentrations of 200, 280, 300, and 440 ng/mL. The mean and median concentrations of methadone detected in this study are 305 and 290 ng/mL, respectively.

5. Discussion

In this study we have not distinguished between illicit and licit drugs. This is because, in terms of driver impairment, any substance that can interfere with the cognitive or physical abilities required to operate a vehicle can produce qualitatively the same effects irrespective of whether the substance was obtained legitimately by prescription or not. Interpretation of the frequency distributions of the drug concentrations given in Figs. 3–8 is complicated by the possibility of drug–drug interactions (e.g. when taken with alcohol), the delay between sampling and analysis (2–4 weeks) and the development of drug tolerance.¹⁴ In addition, the time between arrest and blood sampling varies from case-to-case depending on the circumstances, such as geographic location and the availability of the FME. Usually, little is known about the dose taken, the administration method or the time of intake relative to the time of driving or arrest.

In the case of prescription drugs, such as diazepam, a number of additional factors complicate interpretation, including: chronic dosing (impairment due to diazepam is thought to be mostly due to the accumulation of active metabolites⁵⁵); poor compliance with prescription directions in some patients (i.e. taking too many tablets, obtaining multiple prescriptions from different medical practitioners); genetic differences in drug metabolism and elimination; cross-tolerance; hysteresis and an increasing trend of buying prescription-only medicines over the internet, which are likely to be abused.⁴⁶ The presence of underlying health problems can also complicate interpretation of prescription drug concentrations. It is likely that the illnesses (anxiety, depression, insomnia) for which benzodiazepines are prescribed will have deleterious impacts on driving.⁵⁵ Correct therapeutic use of drugs such as benzodiazepines and methadone may present less of a hazard to traffic safety than that posed by untreated drivers.⁵⁵ For those patients taking prescription medications under medical supervision, tolerance to side-effects such as sedation will normally develop rapidly, and patients learn to recognise their reaction to the drug(s).

In this original communication, we are able to put the concentrations of drugs of abuse observed in drivers in England & Wales within the general context of known therapeutic or abuse

Table 3
Concentrations of mephedrone and case details, concentrations in ng/mL.

Case	Concentration of mephedrone	Driver age	Driver gender	Observations	Other drugs indicated ^a	Reason for suspecting mephedrone
1	39	23	Male	Unsteady on feet, dilated pupils, drunkenness, slow speech	Diazepam, nordiazepam, temazepam	Driver found with white powder confirmed to be methylmethcathinone and 1-naphyrone
2	40	22	Male	Slumped across steering wheel, drooling, difficult to wake, dilated pupils	None	None given
3	56	38	Male	Thirst, drowsiness and hyperactivity	Cannabis	Driver stated he had taken 'NRG-1' or naphyrone
4	110	25	Male	Drowsiness, thirst, hyperactivity	MDA, MDMA, cocaine, cannabis	None given
5	350	21	Male	Dilated pupils	None	Driver stated he had taken 'MCAT'
6	370	19	Male	Chewing gums, twitchy, fidgety, dilated pupils, hyperactivity, thirst	MDMA	Driver stated he had taken 'meow meow'

^a Drugs indicated on EIA, confirmed in the sample by GC–MS or indicated on the submission paperwork by police.

Table 4

Concentrations of GHB and case details, concentrations in µg/mL.

Case	Concentration of GHB	Driver age	Driver gender	Observations	Time delay	Reason for suspecting GHB
1	76	Unknown	Female	Convulsions and drowsiness, loss of control of motor functions	None given	None given
2	84	41	Male	Contracted pupils, delirium, hyperactivity, drowsiness, convulsions, sweating, bloodshot eyes	3 h 2 min	None given
3	96	35	Male	Unsteady, slurred speech, incoherent, agitated, dilated pupils which were unresponsive to light	1 h 54 min	Driver found with a clear bottle of liquid, intelligence, stated he had taken GHB
4	156	Unknown	Male	Hyperactivity, dilated pupils, drowsiness, sweating, bloodshot eyes	None given	Driver found with a clear liquid, stated he had taken GHB
5	188	18	Male	None given	3 h	Driver mentioned GHB at time of arrest

concentrations from toxicological references,^{29,56} and the existing data reported for drug-impaired drivers.

5.1. Alcohol

The mean ($N = 112$) and median blood alcohol concentrations in this study are 120 and 110 mg%, respectively. These values correspond to approximately 1.5 times the legal limit for driving of 80 mg% in the UK. 89 out of the 112 drivers positive for alcohol in this study (79%) were found to be over the legal limit.

5.2. Amphetamine

The mean and median concentrations of amphetamine in this study are 496 and 360 ng/mL ($N = 39$). Both concentrations are higher than those associated with therapeutic use of the drug (20–200 ng/mL²⁹) and only 31% of amphetamine-positive cases in this study have concentrations consistent with therapeutic use. Amphetamine is prescribed in the UK for attention deficit hyperactivity disorder and narcolepsy and this is associated with therapeutic concentrations of ~50 ng/mL (the lowest concentration

Table 5

Concentrations of ketamine and case details, concentrations in ng/mL.

Case	Concentration of ketamine (norketamine)	Driver age	Driver gender	Observations	Other drugs indicated ^a	Reason for suspecting ketamine
1	340 (560)	25	Male	Contracted pupils, thirst, hyperactivity, drowsiness, sweating, bloodshot eyes	MDMA, MDA, amphetamines, cannabis	Driver stated he taken drugs at a rave and had powder residue on nose
2	180 (200)	23	Male	Aggressive, dilated pupils, violence, spaced out	Cannabis	Driver stated he had taken ketamine, white powder found in vehicle and around nose
3	430 (810)	20	Male	Delirium, dilated pupils, unable to stand, unintelligible speech	Cannabis	Driver stated he had taken ketamine, white powder found in vehicle and around nose
4	550 (420)	28	Male	Thirst, dilated pupils	Zopiclone, morphine, diazepam, codeine	Driver stated he had taken ketamine, white powder found in vehicle
5	300 (600)	19	Male	Contracted pupils, drowsy, unsteady on feet, slurred speech	Methylamphetamines, cannabis	Driver stated he had taken ketamine
6	170 (190)	19	Female	Appeared intoxicated	None	Driver stated she had taken ketamine, white powder around nose
7	570 (400)	22	Male	Erratic driving, weaving, struggling to stand up, contracted pupils, unintelligible speech, thirst, hyperactivity	Mephedrone, cannabis	Driver found with wraps of a white powder which contained ketamine and mephedrone
8	290 (700)	26	Male	Dilated pupils, slurred speech, unable to stand, incoherent, runny nose, red nostrils	BZE and/or cocaine	Driver stated he had taken ketamine
9	850 (590)	24	Male	Contracted pupils, drowsy, incoherent, unsteady on feet	None	Driver stated he had taken ketamine
10 ^b	600 (1400)	20	Male	Slow driving, slurred speech, vacant expression, drowsiness	BZE and/or cocaine	Driver stated he had taken ketamine
11 ^b	600 (700)	20	Male	Dilated pupils, bloodshot eyes, runny nose, incoherent speech, unable to keep eyes open, failure to acknowledge presence of police officer	None	Driver stated he had taken ketamine
12 ^b	500 (1000)	20	Male	Failed FIT	None	Driver stated he had taken ketamine, drug found in vehicle
13	220 (190)	36	Male	None given	None	White powder on nose and sleeve
14	300 (850)	22	Male	Dilated pupils, drowsy, slurred speech, unsteady on feet	None	Driver stated he had taken ketamine
15 ^c	—	20	Male	Bloodshot eyes, slurred speech, dilated pupils, unsteady, swerving across road, speeding up and slowing down	None	White powder around nose

^a Drugs indicated on EIA, confirmed in the sample by GC–MS or indicated on the submission paperwork by police.

^b Cases 10–12 all involved the same suspect who was an habitual ketamine user and was apprehended three times in one month.

^c Concentrations of ketamine and norketamine not quantified.

seen in this study is 60 ng/mL). In addition, a number of other legitimate medications are also metabolised to amphetamine.⁴⁷

The mean and median values sit between those reported in the literature: in Scotland, Ledingham¹² reported two cases of drug driving with a mean amphetamine concentration of 1000 ng/mL and Seymour and Oliver⁷ reported three cases where the mean amphetamine concentration was 500 ng/mL; in Sweden, a study of 6613 drug-impaired drivers positive for amphetamine reported mean and median concentrations of 890 and 700 ng/mL respectively,¹⁴ and in a further 300 Swedish drivers positive for amphetamine, the mean and median concentrations were 1000 and 900 ng/mL¹⁵; in 128 drivers positive for amphetamine in Finland the median concentration was 455 ng/mL²⁴; in a study of 878 cases of driving under the influence of amphetamine in Norway, the median blood amphetamine concentration was 520 ng/mL⁴⁸; in two studies in the Netherlands the mean and median amphetamine concentrations were 290 and 165 ng/mL, respectively ($N = 81$) in the first²⁶ and the median concentration was 220 ng/mL ($N = 208$) in the second²⁵ (no mean was reported). In a study of 16 drug drivers positive for amphetamine in Switzerland, the mean and median concentrations were 63 and 54 ng/mL, respectively.²⁷

The maximum amphetamine concentration in this study is 1600 ng/mL which is a level associated with fatalities,²⁹ although an 'abnormally high' concentration of amphetamine was considered to be >5000 ng/mL by Jones and Holmgren.¹⁴ However, even very low measured concentrations of amphetamine can correspond to impaired driving ability due to the fatigue and excessive exhaustion caused by binge use.^{15,47}

5.3. MDMA

The mean and median concentrations of MDMA found in this study are 256 and 230 ng/mL, respectively. These values are slightly lower than those reported in the literature: in Scotland, in a study of three drug-driving cases positive for MDMA the mean concentration was 330 ng/mL¹²; in two papers from the Netherlands, in 87 drivers positive for MDMA, the mean and median concentrations were 352 and 280 ng/mL,²⁶ and in 360 drug-impaired drivers positive for MDMA the median concentration was 330 and mean 440 ng/mL²⁵; in a study of 28 drug-impaired drivers positive for MDMA in Switzerland, the mean and median concentrations were 388 and 218 ng/mL.²⁷

The single concentration of MDA measured in this study (50 ng/mL), is slightly lower than the mean MDA concentration of 63 ng/mL observed in 52 drug-impaired drivers positive for MDA in the Netherlands.²⁶

5.4. Benzodiazepines

The metabolic pathways of common benzodiazepines are interconnected, making interpretation of concentrations somewhat challenging. For example, the presence of oxazepam and temazepam in a blood sample could reflect a number of scenarios: use of diazepam only; use of oxazepam and temazepam; use of temazepam only or a combination of the above.

5.4.1. Diazepam & nordiazepam

Both diazepam and its pharmacologically active metabolite nordiazepam are frequently encountered in blood samples from suspected drug-impaired drivers. The mean and median concentrations of diazepam in this study are 895 and 560 ng/mL and for nordiazepam 1013 and 575 ng/mL. The mean diazepam concentration is consistent with therapeutic use of the drug (range: 125–500 ng/mL in plasma⁵⁶) and 74% of drivers in this study have concentrations of diazepam either below or within the therapeutic

range. For nordiazepam, both concentrations exceed therapeutic concentrations (range: 200–1800 ng/mL in plasma⁵⁶) although 45% of drivers in this study were either below or within the therapeutic range. It should be noted that there is considerable overlap between therapeutic and abuse concentrations for diazepam.

Compared to those reported in the literature, the values for both diazepam and nordiazepam in this study are high: in Scotland, Ledingham¹² reported 22 cases of drug driving positive for diazepam with mean values of 540 ng/mL (diazepam) and 690 ng/mL (nordiazepam $N = 12$). Seymour and Oliver⁷ reported 224 cases positive for diazepam with a mean diazepam level of 800 ng/mL and a mean nordiazepam level of 700 ng/mL ($N = 211$); in a survey of 166 drug-impaired drivers positive for diazepam in the Netherlands, the mean and median concentrations of diazepam were 464 and 277 ng/mL; in the same study, 197 of those drivers also tested positive for nordiazepam with mean and median concentrations of 639 and 260 ng/mL²⁶; in a study of drug-impaired drivers in Norway, single-dose users of diazepam had mean diazepam and nordiazepam concentrations of 532 and 80 ng/mL, respectively, and daily-dose users of diazepam had diazepam and nordiazepam concentrations of 396 and 376 ng/mL, respectively,²⁰ in a study of 10 drug drivers in Switzerland who tested positive for diazepam, the mean and median concentrations of diazepam were 279 and 200 ng/mL; in the same study the mean and median concentrations of nordiazepam were 492 and 305 ng/mL, respectively ($N = 24$).²⁷ An 'unusually high' concentration of diazepam was considered to be >1100 ng/mL by Jones et al.¹⁶ which corresponds to 22% of the cases in this study.

The ratio of diazepam to nordiazepam can indicate whether or not the concentrations measured are consistent with recent or non-recent use. A ratio of:

- <1 (measured in 50% of the samples in this study) may indicate non-recent use;
- ~1 (measured in 7% of samples in this study) indicates regular use of diazepam, as daily use causes nordiazepam to accumulate;
- >3 (measured in 25% of samples) indicates acute and/or recent use.

The mean diazepam-to-nordiazepam ratio in this study is 3.20 which is higher than the mean ratio of 1.94 reported for 13 drivers positive for diazepam in Sweden.¹⁶ Although the mean ratio suggests acute or recent use, Fig. 5 demonstrates the non-recent use of diazepam on the part of the majority of drivers in this study.

5.4.2. Oxazepam

The mean and median concentrations of oxazepam in this study are 391 and 370 ng/mL. Both values are consistent with therapeutic use of oxazepam itself (range: 100–2000 ng/mL⁵⁶) but also with chronic daily therapeutic use of diazepam, albeit at the high end of the range (50–400 ng/mL²⁹). 86% of cases in this study fall either within or below these concentrations, however the profile of results in the seven cases where a concentration of oxazepam was measured, all indicate that oxazepam was present as a breakdown product of diazepam and/or temazepam and was not present due to the use of oxazepam itself.

The concentrations in this study are low compared to those reported in the literature: McLinden⁴⁹ reported 14 cases of drug-impaired driving in Australia where the driver tested positive for oxazepam, and the mean concentration was 2464 ng/mL; in a study of 263 drug-impaired drivers positive for oxazepam in the Netherlands the mean and median concentrations of oxazepam were 986 and 410 ng/mL, respectively²⁶; in a study of 10 drug-impaired drivers who tested positive for oxazepam in Switzerland

the mean and median concentrations of oxazepam were 614 and 230 ng/mL, respectively.²⁷

5.4.3. Temazepam

The mean and median concentrations of temazepam in this study are 1245 and 400 ng/mL, respectively. The mean concentration is much higher than that associated with both therapeutic use of temazepam itself (range: 300–900 ng/mL in plasma⁵⁶) and chronic daily therapeutic use of diazepam, which can also produce a significant concentration of temazepam in the bloodstream (range: 100–600 ng/mL in plasma²⁹). 60% of cases in this study are consistent with therapeutic use of temazepam and 67% are consistent with use of diazepam.

The mean concentration of temazepam found in this study lies between those reported in the literature: in Scotland, Ledingham¹² reported the results for 17 drivers positive for temazepam and a mean temazepam blood concentration of 920 ng/mL, and Seymour and Oliver⁷ reported 266 cases positive for temazepam where the mean temazepam blood concentration was 1900 ng/mL (it should be noted that much higher maximum concentrations of temazepam e.g. 23,140 ng/mL were included in this mean); a study of 135 drug-impaired drivers who tested positive for temazepam in the Netherlands reported mean and median temazepam concentrations of 324 and 62 ng/mL, respectively.²⁶

5.4.4. Alprazolam

The mean and median concentrations of alprazolam found in this study are 141 and 70 ng/mL, respectively. Both values are higher than those associated with therapeutic use of alprazolam (range: 20–40 ng/mL in plasma⁵⁶) and therefore consistent with abuse of the drug. Only 2 of the 11 concentrations measured were within or below a therapeutic concentration of alprazolam. This is perhaps not surprising as alprazolam is not prescribed on the National Health Service in the UK, although it is available via private prescription. Alprazolam is frequently seen as an adulterant in illicit heroin in this laboratory, and alprazolam was detected with opiates in five cases in this study. However, due to the low purity of illicit heroin, and the short half-life of morphine compared to alprazolam, it is possible that the concentration of morphine may have fallen below the cut-off value by the time of sampling in the other cases. Although there is very little information on alprazolam concentrations in drivers in the literature, the values in this study are much lower than those found in a study of two drivers positive for alprazolam in the Netherlands, where both the mean and median concentration was 385 ng/mL²⁶

5.5. Cocaine and benzoylecgonine

5.5.1. Cocaine

The mean and median concentrations of cocaine found in this study are 53 and 25 ng/mL, respectively, and these values are low compared to those reported in the literature: in 61 blood samples positive for cocaine and BZE taken from drug-impaired drivers in Sweden, the mean and median cocaine concentrations were 95 and 70 ng/mL, respectively,¹³ in a study of 336 drivers positive for cocaine in the Netherlands, the mean and median cocaine concentrations were 85 and 50 ng/mL, respectively²⁶; and in a study of 20 drug-impaired drivers in Switzerland, the mean and median concentrations of cocaine were 109 and 50 ng/mL, respectively.²⁷

5.5.2. Benzoylecgonine

Whilst this metabolite of cocaine is not pharmacologically active, and its presence per se does not pose a particular problem for traffic safety,¹³ the come-down stage of cocaine use (which

could be indicated by a positive result for BZE) is not compatible with driving. Specimens containing BZE verify that cocaine was taken some time earlier, whilst samples containing cocaine indicate fairly recent use. However, there is a risk that cocaine may be converted to BZE¹³ or methylecgonine²⁸ in blood samples depending on specimen preservation and storage conditions.

The overall mean and median concentrations of BZE in this study are 677 and 420 ng/mL. These values are between those reported in the literature: for 55 drug-impaired drivers positive for BZE in Switzerland the mean and median BZE concentrations were 515 and 250 ng/mL, respectively,²⁷ in a study of 361 drivers positive for BZE in the Netherlands, the mean and median concentrations of BZE were 1104 and 760 ng/mL, respectively.²⁶

For BZE detected with cocaine, the mean and median BZE concentrations in this study are 1013 and 740 ng/mL. These values are very similar to those reported in a study of 61 drug-impaired drivers in Sweden positive for both compounds where the mean and median BZE concentrations were 1010 and 700 ng/mL, respectively.¹³

For BZE detected alone, the mean and median concentrations in this study are 355 and 230 ng/mL. These are high compared to the mean and median concentrations of BZE of 200 and 130 ng/mL reported for 96 drug-impaired drivers positive for BZE only in Sweden.¹³

5.6. Opiates

5.6.1. Morphine

Morphine is commonly found in the blood of impaired drivers,¹⁷ however its presence can reflect a number of situations including the use of illicit heroin, the use of medications containing codeine, the use of morphine itself, or a combination of the above. The mean and median concentrations of free morphine in this study are 66 and 40 ng/mL, respectively. These concentrations are consistent with therapeutic use of morphine (range: 10–100 ng/mL²⁹) and 90% of the cases in this study fall either below or within the therapeutic range. However, there is significant overlap between therapeutic concentrations of morphine and those arising through the use of illicit heroin.

The concentrations found in this study lie between those reported in the literature: in Scotland, Ledingham¹² reported one case of drug driving positive for morphine with a concentration of 80 ng/mL, and Seymour and Oliver reported 97 cases positive for morphine with a mean morphine concentration of 70 ng/mL⁷; in a study of 184 drug-impaired drivers positive for morphine in the Netherlands, the mean and median morphine concentrations were 52 and 40 ng/mL respectively,²⁶ and in 2029 drug-impaired drivers positive for morphine in Sweden the mean and median concentrations of morphine were 46 and 30 ng/mL, respectively¹⁷; in a study of 32 drug-impaired drivers positive for morphine in Switzerland, the mean and median morphine concentrations were 19 and 10 ng/mL²⁷; in 979 drug-impaired drivers positive for morphine in Sweden the mean and median morphine concentrations were 30 and 51 ng/mL⁵⁰; in Norway the mean and median concentrations of morphine in 98 drug-impaired drivers positive for morphine were 31 and 27 ng/mL.⁵¹

5.6.2. Codeine

The presence of codeine can be due to the use of prescription or over-the-counter codeine itself or due to the use of illicit heroin, or a combination of both scenarios. The mean and median concentrations of free codeine in this study are 348 and 60 ng/mL. The mean codeine concentration is higher than that associated with therapeutic use (range: 30–100 ng/mL²⁹) although 78% of the cases in this study fall either below or within the therapeutic range. The

mean and median concentrations of codeine in this study are higher than those reported in the literature: in 1391 drug-impaired drivers positive for codeine in Sweden the mean and median codeine concentrations were 47 and 10 ng/mL, respectively¹⁷; in 784 drug-impaired drivers positive for codeine in Sweden, the mean and median codeine concentrations were 68 and 20 ng/mL, respectively; in 21 codeine-positive drug-impaired drivers in Switzerland both the mean and median codeine concentrations were 5 ng/mL²⁷.

Low concentrations of codeine may be present as a consequence of acetyl-codeine breakdown, since codeine is a prominent alkaloid in raw opium.¹⁷ In six of the nine cases positive for codeine in this study, morphine was also present, and the codeine-to-morphine ratios have been calculated for each of these cases. A morphine:codeine value of >1 suggests heroin use⁵⁰ as is the situation for three of the six cases in this study. The mean and median ratios are 3.2 and 2.2 which are low compared to the values of 6.5 and 6.0 reported for 833 drug-impaired drivers in Sweden.¹⁷

5.6.3. Dihydrocodeine

The mean and median concentrations of dihydrocodeine in this study are 410 and 190 ng/mL. The mean is higher than those concentrations associated with therapeutic use (50–200 ng/mL²⁹) however, two of the three cases were within the therapeutic range.

The mean and median in this study are lower than the mean dihydrocodeine concentrations found in two studies in Scotland. In 26 drug-impaired drivers a mean dihydrocodeine concentration of 700 ng/mL was measured,⁷ and in a further seven drug-impaired drivers positive for dihydrocodeine, the mean concentration was 2850 ng/mL¹².

5.7. Mephedrone

The mean and median concentrations of mephedrone determined in this study are 161 and 83 ng/mL, respectively. There is very little information on this new drug in the literature, however the mean is lower than the level found in the blood of a driver fatally injured in a road traffic accident in Scotland (230 ng/mL)⁴² but higher than a serum concentration of 150 ng/mL that has also been reported for a recreational mephedrone user.⁵³ Unfortunately, direct comparison of concentrations is not possible as there are no reports in the literature of whole-blood concentrations of mephedrone in drug-impaired drivers. However, the effects of mephedrone are known to include a dry mouth, agitation (restlessness) and dilated pupils^{52,53} observations made in cases in this study by police officers at the time of arrest (see Table 3).

The concentrations measured in this study, may be an underestimate, as mephedrone has been found to be unstable in whole blood samples under neutral and basic conditions, even in the presence of NaF.³⁰

5.8. GHB/GBL

The mean and median concentrations of GHB in this study are 119 and 100 µg/mL respectively and are within the range associated with the use of GHB as a hypnotic to induce light sleep (range: 52–156 µg/mL²⁹); four of the five concentrations of GHB measured in this study are within this range. The other concentration of GHB measured was 188 µg/mL, which is associated with therapeutic use of GHB to induce moderate sleep (range: 156–260 µg/mL²⁹). However, GHB has an extremely short half-life of 30–40 min thus any delay between the incident and sampling could result in a significant decrease in GHB blood concentration.¹⁸ The time delays in the cases in the study, where recorded, were usually 2–

3 h (see Table 4), indicating that the concentrations of GHB measured were very likely much higher at the time of driving. Some of the observations recorded by the police at the time of arrest (Table 4) agree with those reported in the literature: drowsy; incoherent; bloodshot eyes and dilated pupils that were unresponsive to light; unsteady co-ordination; slurred speech; sweating.^{18,23}

The mean and median values reported in this study are higher than those reported in the literature: Couper and Logan²³ reported 13 cases of drug driving in the USA where the driver was positive for GHB and the mean and median concentrations were 87 and 95 µg/mL, respectively; Jones et al.¹⁸ analysed 473 blood samples positive for GHB taken from drug-impaired drivers in Sweden and the mean and median GHB concentrations were 90 and 84 ng/mL, respectively; a further study by the same authors of 548 samples positive for GHB, reported mean and median GHB concentrations of 89 and 82 ng/mL, respectively.¹⁹

5.9. Ketamine

The mean and median concentrations of ketamine found in this study are 421 and 385 ng/mL, respectively, and the mean and median concentrations of norketamine are 605 and 410 ng/mL, respectively. When ketamine is used for anaesthesia, wakefulness is associated with patients with a plasma ketamine concentration of ~600 ng/mL.²⁹ Unfortunately, there is very little data in the literature on the concentrations of ketamine found in whole blood following abuse of the drug, although urine and oral fluid concentrations have been reported for ketamine abusers in Hong Kong.⁵⁴ In the same study, the ketamine users took part in a FIT and the study authors noted the following observations: bloodshot eyes and dilated pupils; runny nose; traces of white powder in nasal cavities; impaired divided attention; swaying; difficulty walking. The observations noted in Table 5 are very similar, although it should be pointed out that cannabis can also produce bloodshot eyes (e.g. Case 1). There are no reports in the literature of whole-blood concentrations of ketamine in drug-impaired drivers.

5.10. Methadone

The mean and median concentrations of methadone quantified in this study are 305 and 290 ng/mL, respectively. Both values are consistent with chronic therapeutic use of methadone (i.e. for the treatment of opiate dependence, range: 280–790 ng/mL^{9,29}) and all four cases in this study are within the therapeutic range.

The mean and median values lie between those reported in the literature: in a study of 104 drug-driving cases where the sample was positive for methadone in Norway, the median concentration of methadone was 309 ng/mL²²; in a study of 88 drug-impaired drivers positive for methadone in the Netherlands, the mean and median concentrations of methadone were 151 and 120 ng/mL²⁶; in Scotland, Seymour and Oliver reported 35 cases of drug driving positive for methadone, with a mean methadone concentration of 100 ng/mL⁷; in Switzerland Augsburg et al. reported methadone concentrations for 31 drug-impaired drivers, with mean and median values of 165 and 110 ng/mL, respectively.²⁷

5.11. Phenazepam

The low-dose benzodiazepine drug phenazepam [7-bromo-5-(2-chlorophenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one] is prescribed in Russia for the short-term treatment of anxiety disorders, and as an anticonvulsant.⁵⁷ It was controlled in the UK as a Class C drug in June 2012. Phenazepam is growing in popularity as a drug of abuse and is obtained *via* direct purchase from internet

websites.⁵⁸ Phenazepam was confirmed in 13 drug-driving cases, and in 3 of these cases a request was made for the quantification of phenazepam. The concentrations of phenazepam detected in these 3 cases were 120, 180 and 870 ng/mL of blood.

Phenazepam has also been quantified in drug-driving cases in Finland; in 2003, 20 drug-impaired drivers were positive for phenazepam with a reported range of concentrations 18–400 ng/mL.⁵⁹

6. Conclusions

We have determined the concentrations of alcohol and drugs of abuse in 376 suspected drug-driving cases in England & Wales between February 2010 and March 2011.

The drug most frequently observed within this study was cocaine and/or its metabolite benzoylecgonine followed by diazepam and its metabolite nordiazepam. However, the number of cases that satisfied the study criteria was fewer than half of the total number of drug-driving cases submitted to the FSS, therefore overall prevalence conclusions regarding drug use and driving can not be drawn from this study. The mean and median blood alcohol concentrations were 120 and 110 mg%, respectively which are in excess of the prescribed limit for driving in the UK of 80 mg%.

The concentrations and case details for ketamine, mephedrone and phenazepam found in drivers in England & Wales are reported in this study. This is an important contribution to the drug-driving literature as there is currently no data on the prevalence or concentrations of these drugs in drivers, despite recent evidence suggesting there has been a surge in their use.² However, these substances do not produce a positive result on the EIA kits used (unless present at a very high level where there may be some cross-reaction of mephedrone metabolites with the amphetamine antibodies) and are usually only confirmed in drug-driving cases if the police have specific intelligence that points to their use and/or the EIA screen has failed to detect any other drugs that could explain the driver's behaviour. As this further testing attracts an additional cost to police, and which may not be authorised, the true prevalence of these drugs in drug-impaired drivers is probably underestimated by this study.

The concentrations of the less common drugs of abuse alprazolam and GHB found in drivers in England & Wales are also reported in this study. There is very little data in the drug-driving literature regarding these drugs, and this communication reports the first UK drug-driving data for alprazolam and GHB.

The differences in drug concentrations across different countries are most likely due to different driving and medication habits between countries.

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Conflict of interest

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References

- Consensus Development Panel. *J Am Med Assoc* 1985;**254**:2618–21.
- Oliver JS, Seymour A, Wylie FM, Torrance H, Anderson RA. *Monitoring the effectiveness of UK field impairment tests*. London: Department for Transport; 2006.
- Jackson PG, Hilditch CJ. *A review of evidence related to drug driving in the UK: a report submitted to the North review team*. London: Department for Transport; 2010.
- Rudram D. Drugs and driving in the United Kingdom. *Can Soc Forensic Sci J* 1999;**32**:47–53.
- Albery IP, Strang J, Gossop M, Griffiths P. Illicit drugs and driving: prevalence, beliefs and accident involvement among a cohort of current out-of-treatment drug users. *Drug Alcohol Depend* 2000;**58**:197–204.
- Elliott S, Woolacott H, Braithwaite R. The prevalence of drugs and alcohol found in road traffic fatalities: a comparative study of victims. *Sci Justice* 2009;**49**:19–23.
- Seymour A, Oliver JS. Role of drugs and alcohol in impaired drivers and fatally injured drivers in the Strathclyde police region of Scotland, 1995–1998. *Forensic Sci Int* 1999;**103**:89–100.
- Buttress SC, Tunbridge RJ, Oliver JS, Torrance H, Wylie F. The incidence of drink and drug driving in the UK – a roadside survey in Glasgow. In: Presented at the 17th international conference on alcohol, drugs and traffic safety. Glasgow, UK; 2004.
- Ingram D, Lancaster B, Hope S. *Recreational drugs and driving: prevalence survey*. Edinburgh: The Scottish Executive Central Research Unit; 2000.
- Chatterton CN, Osselson DM. Drug use in UK drivers: concentrations of benzodiazepines and opioids in whole blood specimens collected from drivers suspected of driving whilst impaired through drugs in England and Wales. In: Presented at the annual meeting of the Society of Forensic Toxicologists. Phoenix, Arizona, USA; 2008.
- Chatterton CN, Osselson DM. Drug use in UK drivers: concentrations of amphetamine, methylenedioxymethyl-amphetamine (MDMA) and cocaine in whole blood specimens collected from drivers suspected of driving whilst impaired through drugs in England and Wales. In: Presented at the Society of Forensic Toxicologists (SOFT) annual meeting. Raleigh-Durham, North Carolina, USA; 2007.
- Ledingham D. Drugs and driving: a retrospective study of the analyses of blood and urine specimens submitted to the Lothian and Borders Police Forensic Laboratory. *J Clin Forensic Med* 1999;**6**:133–40.
- Jones AW, Holmgren A, Kugelberg FC. Concentrations of cocaine and its major metabolite benzoylecgonine in blood samples from apprehended drivers in Sweden. *Forensic Sci Int* 2008;**177**:133–9.
- Jones AW, Holmgren A. Abnormally high concentrations of amphetamine in blood of impaired drivers. *J Forensic Sci* 2005;**50**:1215–20.
- Jones AW. Age- and gender-related differences in blood amphetamines concentrations in apprehended drivers: lack of association with clinical evidence of impairment. *Addiction* 2007;**102**:1085–91.
- Jones AW, Holmgren A, Holmgren P. High concentrations of diazepam and nordiazepam in blood of impaired drivers: association with age, gender and spectrum of other drugs present. *Forensic Sci Int* 2004;**146**:1–7.
- Jones AW, Holmgren A, Kugelberg FC. Driving under the influence of opiates: concentration relationships between relationships between morphine, codeine, 6-acetyl morphine, and ethyl morphine in blood. *J Anal Toxicol* 2008;**32**:265–72.
- Jones AW, Holmgren A, Kugelberg FC. Gamma-hydroxybutyrate concentrations in the blood of impaired drivers, users of illicit drugs, and medical examiner cases. *J Anal Toxicol* 2007;**31**:566–72.
- Jones AW, Holmgren A, Kugelberg FC. Driving under the influence of gamma-hydroxybutyrate (GHB). *Forensic Sci Med Pathol* 2008;**4**:205–11.
- Bramness JG, Skurtveit S, Mørland J. Testing for benzodiazepine inebriation-relationship between benzodiazepine concentration and simple clinical tests for impairment in a sample of drugged drivers. *Eur J Clin Pharmacol* 2003;**59**:593–601.
- Sturtveit S, Abotnes B, Christophersen AS. Drugged drivers in Norway with benzodiazepine detections. *Forensic Sci Int* 2002;**125**:75–82.
- Mørland J, Ripel A, Øgaard T. Methadone detection in blood samples from apprehended drugged drivers. In: Proceedings of the 16th international conference on alcohol, drugs and traffic safety. Montreal, Canada; 2002.
- Couper FJ, Logan BK. GHB and driving impairment. *J Forensic Sci* 2001;**46**:919–23.
- Engblom C, Gunnar T, Rantanen A, Lillsunde P. Driving under the influence of drugs—amphetamine concentrations in oral fluid and whole blood samples. *J Anal Toxicol* 2007;**31**:276–80.
- Verschraagen M, Maes A, Ruiter B, Bosman IJ, Smink BE, Luthof KJ. Post-mortem cases involving amphetamine-based drugs in the Netherlands comparison with driving under the influence cases. *Forensic Sci Int* 2007;**170**:163–70.
- Smink BE, Ruiter B, Luthof KJ, Zweipfenning PGM. Driving under the influence of alcohol and/or drugs in the Netherlands 1995–1998 in view of the German and Belgian legislation. *Forensic Sci Int* 2001;**120**:195–203.
- Augsburger M, Donzé N, Ménétrey A, Brossard C, Sporkert F, Grioud C, et al. Concentration of drugs in blood of suspected impaired drivers. *Forensic Sci Int* 2005;**153**:11–5.
- Dick GL, Stone HM. Alcohol loss arising from microbial contamination of drivers' blood specimens. *Forensic Sci Int* 1987;**34**:17–27.

29. Baselt RC. *Disposition of toxic drugs and chemicals in man*. 5th ed. California: Chemical Toxicology Institute; 2000.
30. Sørensen LK. Determination of cathinones and related ephedrine in forensic whole-blood samples by liquid-chromatography–electrospray tandem mass spectrometry. *J Chromatogr B* 2011;**879**:727–36.
31. Jones AW. *The relationship between blood alcohol concentration (BAC) and breath alcohol concentration (BrAC): a review of the evidence*. London: Department for Transport; 2010.
32. Zacny JP. A review of the effects of opioids on psychomotor and cognitive functioning in humans. *Exp Clin Psychopharmacol* 1995;**3**:432–66.
33. *Magistrates' court sentencing guidelines*. London: Sentencing Guidelines Council; 2009. p. 124.
34. Couper FJ, Logan BK. *Drugs and human performance fact sheets*. Washington DC: National Highway Traffic Safety Administration; 2004. p. 61.
35. Logan BK, Couper FJ. 3,4-Methylenedioxymethamphetamine (MDMA, ecstasy) and driving impairment. *J Forensic Sci* 2001;**46**:1426–33.
36. Drummer OH. Benzodiazepines—effects on human performance and behavior. *Forensic Sci Rev* 2002;**14**:1–14.
37. Isenschmid DS. Cocaine—effects on human performance and behaviour. *Forensic Sci Rev* 2002;**14**:61–100.
38. Borgeat A. Do opioids affect the ability to drive safely? *J Pain Palliat Care Pharmacother* 2010;**24**:167–9.
39. Galski JB, Williams JB, Ehle HT. Effects of opioids on driving ability. *J Pain Symptom Manage* 2000;**19**:200–8.
40. Stout PR, Farrell LJ. Opioids—effects on human behavior and performance. *Forensic Sci Rev* 2002;**14**:29–59.
41. Controlled drugs excepted from the prohibition on importation, exportation and possession and subject to the requirements of regulations 24 and 26. Misuse of drugs regulations 2001, schedule 5, s. 1(2).
42. Maskell PD, De Paoli G, Seneviratne C, Pounder DJ. Mephedrone (4-methylmethcathinone)-related deaths. *J Anal Toxicol* 2011;**35**:188–91.
43. Li J-H, Vicknasingham B, Cheung Y-W, Zhou W, Nurhidayat AW, Des Jarlais DC, et al. To use or not to use: an update on licit and illicit ketamine use. *Subst Abuse Rehabil* 2011;**2**:11–20.
44. Penning R, Veldstra JL, Daamen AP, Olivier B, Verster JC. Drugs of abuse, driving and traffic safety. *Curr Drug Abuse Rev* 2010;**3**:23–32.
45. Mozayani A. Ketamine-effects on human performance and behaviour. *Forensic Sci Rev* 2002;**14**:123–31.
46. North P. *Report of the review of drink and drug driving law*. London: Department for Transport; 2010.
47. Logan BK. Methamphetamine-effects on human performance and behaviour. *Forensic Sci Rev* 2002;**14**:133–51.
48. Gustavsen I, Bramness JG, Mørland J. Impairment related to blood amphetamine concentration in drivers suspected of drug abuse. In: Presented at the 17th international conference on alcohol, drugs and traffic safety. Glasgow, UK; 2004.
49. McLinden VJ. Experiences in relation to drugs/driving offences. *Forensic Sci Soc* 1987;**27**:73–80.
50. Ceder G, Jones AW. Concentration ratios of morphine to codeine in blood of impaired drivers as evidence of heroin use and not medication with codeine. *Clin Chem* 2001;**47**:1980–4.
51. Bachs L, Bramness J, Skurtveit S, Mørland J. Morphine blood concentration and clinical impairment in a population of drugged drivers. In: Presented at the 17th international conference on alcohol, drugs and traffic safety. Glasgow, UK; 2004.
52. Wood DM, Davies S, Puchnarewicz M, Button J, Archer R, Ramsey J, et al. Recreational use of mephedrone (4-methylmethcathinone, 4-MMC) and associated sympathomimetic toxicity. *J Med Toxicol* 2010;**6**:327–30.
53. Schifano F, Albanese A, Fergus S, Stair JL, Deluca P, Corazza O, et al. Mephedrone (4-methylmethcathinone; 'meow meow'): chemical, pharmacological and clinical issues. *Psychopharmacology* 2010;**214**:593–602.
54. Cheng W-C, Ng K-M, Chan K-K, Mok VK-K, Cheung BK-L. Roadside detection of impairment under the influence of ketamine—evaluation of ketamine impairment symptoms with reference to its concentration in oral fluid and urine. *Forensic Sci Int* 2007;**170**:51–8.
55. Friedel B, Staak M. Benzodiazepines and driving. *Rev Contemp Pharmacother* 1992;**3**:415–74.
56. TIAFT drug reference ranges www.tiaft.org.
57. Maskell PD, De Paoli G, Seetohul LN, Pounder DJ. Phenazepam is currently being misused in the UK. *Br Med J* 2011;**343**:d4207.
58. Bailey K, Richards-Waugh L, Clay D, Gebhardt M, Mahmoud H, Kraner JC. Fatality involving the ingestion of phenazepam and poppy seed tea. *J Anal Toxicol* 2010;**34**:527–32.
59. Mykkänen S, Gunnar T, Ariniemi K, Lillsunde P, Krasnova R. Quantitation of phenazepam in blood by GC–MS in positive drug-driving cases in Finland. In: Presented at the annual meeting of the Society of Forensic Toxicologists. Washington DC, USA; 2004.